Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method for increasing the target-specific toxicity of a drug, comprising pretargeting an enzyme to a mammalian target site; and

administering a cytotoxic drug known to act at the target site, or a prodrug form thereof which is converted to the drug *in situ*, which drug is also detoxified to form an intermediate of lower toxicity using said mammal's ordinary metabolic processes, whereby the detoxified intermediate is reconverted to its more toxic form by the pretargeted enzyme and thus has enhanced cytotoxicity at the target site.

2. (Original) The method of claim 1, wherein said enzyme is a glucuronidase.

3. (Original) The method of claim 1, wherein said mammal is a human.

4. (Original) The method of claim 1, wherein said drug is any standard chemotherapeutic agent.

5. (Original) The method of claim l, wherein said prodrug is the cancer chemotherapy agent CPT-11, and said detoxified intermediate is SN-38-glucuronide.

6. (Original) The method of claim 5, wherein an esterase that; cleaves CPT-11 to SN-38 also is pretargeted to said target site.

7. (Original) The method of claim 1, wherein a bispecific MAb (bsMAb) is used to target said enzyme to said target site, wherein one arm of the bsMAb is targeted against a target site antigen and a second arm of the bsMAb is targeted against a low molecular weight hapten, and wherein said enzyme is conjugated to said hapten.

8. (Original) The method of claim 7, wherein a second prodrug cleavage enzyme also is conjugated to said hapten, and wherein the second enzyme conjugate also is pretargeted to said target site.

9. (Original) The method of claim 7, wherein said hapten is DTPA or a DTPA chelate.

10. (Original) The method of claim 8, wherein said hapten is DTPA or a DTPA chelate.

11. (Original) The-method of claim l, wherein additionally, a clearing agent is administered to remove non-targeted pretargeting molecules and/or enzymes from said mammal's circulation prior to administration of said drug or prodrug.

12. (Original) The method of claim 11, wherein said clearing agent is an anti-MAb antibody or an anti-idiotype antibody.

13. (Original) The method of claim 11, wherein said enzyme is conjugated to a hapten and said clearing agent is an antibody that binds said hapten.

14. (Original) The method of claim 11, wherein said enzyme is conjugated to a Mab and said clearing agent is an anti-idiotypic antibody or anti-idiotypic antibody fragment which is specific for the paratope of said Mab.

Claims 15-19 (Canceled).

20. (Previously Presented) A kit for increasing the target-specific toxicity of a drug, comprising:

a. a targeting composition selected from the group consisting of:

an antibody or antibody fragment which specifically binds to a target site, conjugated to an enzyme that converts a detoxified drug to its more cytotoxic form; and

a bispecific antibody or antibody fragment which has at least one binding site specific to the target site and another binding site specific to an enzyme or to a recognition hapten bound to an enzyme, wherein the enzyme converts a detoxified drug to a cytotoxic form, and said enzyme or said enzyme-recognition hapten; and

b. a cytotoxic drug or a prodrug of a cytotoxic drug other than a glucuronide, wherein said cytotoxic drug is converted to a detoxified metabolite by a mammal's ordinary metabolic processes and said detoxified metabolite is converted into said cytotoxic drug by said enzyme,

wherein said enzyme is selected from the group consisting of an abzyme, a mutated form of a natural enzyme, and a synthetic or semi-synthetic catalytic molecule.

21. (Previously Presented) The kit of claim 20, wherein said enzyme is a glycosylase, an esterase, an amidase, or a sulfatase.

22. (Previously Presented) The kit of claim 20, wherein said cytotoxic drug or prodrug is used in cancer chemotherapy.

23. (Previously Presented) The kit of claim 22, wherein said cytotoxic drug or prodrug is a camptothecin or an anthracyline derivative.

24. (Previously Presented) The kit of claim 23, wherein said cytotoxic prodrug is selected from the group consisting of CPT-11, topotecan, DX8951f, rubitecan, doxorubicin, and epirubicin.

25. (Previously Presented) The kit of claim 20, wherein said cytotoxic prodrug comprises a polymer with multiple drug addends.

26. (Previously Presented) The kit of claim 25, wherein said cytotoxic prodrug comprises a polymer bearing camptothecin or anthracucline addends.

27. (Previously Presented) The kit of claim 25, wherein said polymer is a dextran, aminodextran, polyethylene glycol, polylysine, polyaspartic acid, polyglutamic acid or dendrimer.

28. (Currently Amended) ~~The~~ A kit ~~of claim 20, wherein~~ for increasing the target-specific toxicity of a drug, comprising:

a. a targeting composition selected from the group consisting of:

an antibody or antibody fragment which specifically binds to a target site, conjugated to an enzyme that converts a detoxified drug to its more cytotoxic form; and

a bispecific antibody or antibody fragment which has at least one binding site specific to the target site and another binding site specific to an enzyme or to a recognition hapten bound to an enzyme, wherein the enzyme converts a detoxified drug to a cytotoxic form, and said enzyme or said enzyme-recognition hapten; and

b. a cytotoxic drug or a prodrug of a cytotoxic drug other than a glucuronide, wherein said cytotoxic drug is converted to a detoxified metabolite by a mammal's ordinary metabolic processes and said detoxified metabolite is converted into said cytotoxic drug by said enzyme,

wherein said enzyme is selected from the group consisting of an abzyme, a mutated form of a natural enzyme, and a synthetic or semi-synthetic catalytic molecule and said cytotoxic drug or prodrug is used along with a modulating agent, to alter the serum concentration of its detoxified metabolite.

29. (Currently Amended) ~~The~~ A kit ~~of claim 28, wherein said modulating agent is~~ for increasing the target-specific toxicity of a drug, comprising:

a. a targeting composition selected from the group consisting of:

an antibody or antibody fragment which specifically binds to a target site, conjugated to an enzyme that converts a detoxified drug to its more cytotoxic form; and

a bispecific antibody or antibody fragment which has at least one binding site specific to the target site and another binding site specific to an enzyme or to a recognition hapten bound to an enzyme, wherein the enzyme converts a detoxified drug to a cytotoxic form, and said enzyme or said enzyme-recognition hapten; and

b. a cytotoxic drug or a prodrug of a cytotoxic drug other than a glucuronide, wherein said cytotoxic drug is converted to a detoxified metabolite by a mammal's ordinary metabolic processes and said detoxified metabolite is converted into said cytotoxic drug by said enzyme,

wherein said enzyme is selected from the group consisting of an abzyme, a mutated form of a natural enzyme, and a synthetic or semi-synthetic catalytic molecule and said cytotoxic drug or prodrug is used along with cyclosporin A, valproic acid or phenobarbitol, to alter the serum concentration of its detoxified metabolite.

30. (Previously Presented) The kit of claim 20, wherein said enzyme, antibody or fragment, or bispecific antibody or antibody fragment is murine, chimeric, humanized or human in origin.

31. (Previously Presented) The hit of claim 20, wherein said target site is a cancer, an infectious and parasitic lesion, a fibrin clot, a myocardial infarction, an atherosclerotic plaque, a damaged normal cell, a non-cancerous, or a lymphocyte autoreactive clone.

32. (Previously Presented) The kit of claim 20, wherein said antibody or antibody fragment, or said bispecific antibody or antibody fragment specifically binds to a surface receptor that is qualitatively distinct for a cancer cell or quantitatively increased in a cancer cell as compared to a non-cancer cell.

33. (Previously Presented) The kit of claim 32, wherein said receptor is a sheep erythrocyte receptor, a hormone receptor, a transferrin receptor, an Fc immunoglobulin receptor, or a nerve growth factor receptor.

34. (Previously Presented) The kit of claim 33, wherein said hormone receptor is an estrogen receptor.

35. (Previously Presented) The kit of claim 20, wherein said antibody or antibody fragment specifically binds to a marker or a substance produced by or associated with a tumor.

36. (Previously Presented) The kit of claim 35, wherein said marker is a T-cell or B-cell marker associated with lymphomas or leukemias.

37. (Previously Presented) The kit of claim 35, wherein said substance is an antigen associated with myeloma, glioma, or melanoma.

38. (Currently Amended) The kit of claim 20, wherein said antibody or antibody fragment specifically binds to a marker, an antigen or a product produced by or associated with an infectious lesion caused by viral, bacterial, fungal, or parasitic infections.

39. (Previously Presented) The kit of claim 20, wherein said antibody or antibody fragment specifically binds to a CEA antigen.

40. (Previously Presented) The kit of claim 20, further comprising a clearing agent for said enzyme.

41. (Previously Presented) The kit of claim 40, wherein said clearing agent is a secondary antibody reactive with some part of said targeting composition.

42. (Previously Presented) The kit of claim 41, wherein said clearing agent is an intact antibody, a fragment of an antibody, or a derivative of an antibody with mono- or multi-valent binding to another moiety.

43. (Previously Presented) The kit of claim 41, wherein said clearing agent is further substituted with a second agent to enhance circulatory clearance.

44. (Previously Presented) The kit of claim 43, wherein said second agent is a galactosyl residue.

45. (Previously Presented) The kit of claim 40, wherein said clearing agent is a high MW protein-bearing hapten recognized by one of the arms of the bsMAb.

46. (Previously Presented) The kit of claim 45, wherein said protein-bearing hapten is a conjugate comprising human serum albumin and DTPA.

47. (Previously Presented) The kit of claim 46, wherein said hapten is further substituted with a galactosyl residue.

48. (Previously Presented) The method of claim 1, wherein said enzyme is selected from the group consisting of a glycosylase other than a glucuronidase, a sulfatase, an esterase or an amidase.